In the Drawing

Please replace Figures 1 and 4 with the replacement sheets attached hereto.

Remarks

The Amendments

In the Action, the examiner indicated that dependent claims should begin with the phrase "The method" instead of "A method." The claims presented herein have been amended as suggested. The examiner also indicated that multiple dependent claims including the statement "according to any preceding claim" should be reworded. The claims presented herein use different language.

The examiner noted that some sequences in the application did not have sequence identifiers. The specification and Figures 1 and 4 have been amended to include sequence identifiers wherever sequences of more than ten nucleotides or four amino acids appear, and sequences have been added to the sequence listing as necessary. Paper and computer-readable copies of the amended sequence listing are substituted for the original sequence listing by the amendment herein. The substitute Sequence Listing complies with the requirements of 37 CFR §§ 1.821-1.825.

Claim 13 as amended is the sole independent claim pending. In amended claim 13, step (ii) has been amended to recite that the samples of the target are divided into separate reaction compartments as is described at page 6, lines 22-23 and 25-26 of the application. Step (ii) is further amended to recite that the adapter comprises an overhang that is a complementary sequence to the polynucleotide sequence represented by the signal sequence and that the adapter will hybridize to the overhang on the target sample that is to be sequenced only if the sequence of the adapter overhang is complementary to the overhang that is being sequenced. This is described at page 9, lines 25-31 of the application.

Clerical amendments to provide antecedent basis for claim terms include: in claim 8, changing "restriction enzyme recognition sequence" to "restriction site" and in step (ii) of claim 13, changing "adapter overhang sequence" to "adapter overhang"

New claim 16 recites that the combination of all the sequences represented by the signal sequence in each reaction compartment corresponds to all the permutations of a sequence comprising the number of bases in the overhang to be sequenced. Support for this claim is found on page 9, lines 22-23 of the application.

None of the amendments introduces new matter.

Claim 1-7 are cancelled herein. Applicant reserves the right to pursue claims of the same or similar scope in duly filed continuation or continuation-in-part applications.

The Rejection under Section 102(b) Should Be Withdrawn

The examiner rejected claim 13 as being anticipated by Jones *et al.* WO00/39333, asserting that the published application teaches a method for determining the sequence of a polynucleotide comprising i) treating a sample of a double stranded target polynucleotide to create overhangs at each end having defined number of bases in each overhang (page 33, line 17-35, page 54, line 13-22); ii) dividing sample and contacting each sample with a signal sequence and a double stranded adapter sequence and ligating said sequences (page 54, line 19-31); iii) carrying out polymerase chain reaction using primers that hybridize to the ends of the polynucleotide, optionally repeating the steps (page 54, line 32-37); iv) identifying the presence of the signal sequences on the amplified products, in which order, and determining the sequence of the target polynucleotide (page 55, lines 1-6, page 36- lines 24-37).

In response, Applicant notes the Jones *et al.* published application fails to disclose that the binding of the target to the sequence specific adapter is detected with the help of a second adapter (*i.e.*, the signal sequence) that is ligated to the second end of the target as is required by claim 13. Nor does the published application disclose that a subsequent amplification step uses primers that hybridize to both of the adapter sequences.

Claim 13 and its dependent claims as presented herein are therefore novel and the rejection under Section 102(b) should be withdrawn.

The Rejection under Section 103(a) Should Be Withdrawn

The examiner rejected claim 10 as purportedly obvious over Jones *et al.* WO00/39333 in view of Sorge *et al.* U.S. Patent No. 6,017,701. The examiner argued that it would have

been obvious to use 5-methyl-dCTP nucleotides of the U.S. patent (col. 8, lines 46-64, col. 19, lines 27-52) in the method of the published application (described above) and that it would have been obvious that the combination would result in a sensitive and enhanced method for detecting specific target nucleic acid sequences.

In response, Applicant submits that the Jones *et al.* published application does not suggest the method of amended claim 13 (or amended claim 10 dependent thereon) nor does the Sorge *et al.* patent remedy the deficiencies of the published application.

More specifically in the published application, the moiety comprising the magnified tag, (which corresponds to the signal sequence of the present invention) is ligated to the portion of the target polynucleotide that it represents. As sequencing progresses, the signal sequences are added to the sequenced end of the target polynucleotide.

In contrast, in methods of the present invention, the signal sequence hybridizes to the end of the target molecule opposite the end at which the portion of the target sequence that it represents is located. The adapter is ligated to the end of the target polynucleotide to be sequenced and is cleaved after each round of amplification. The adapter, which is complementary to the sequence represented by the signal sequence, will hybridize to the portion of the target that is to be represented by the signal sequence only if the sequence of the adapter is also complementary to this portion of the target sequence. Polymerase amplification can only proceed exponentially if both the adapter and signal sequences are ligated to the target polynucleotide, since both are required for primer recognition. Therefore, the only samples which will be amplified are those wherein the adapter, being complementary to the sequence represented by the signal sequence, is also complementary to the target overhang, thereby identifying the sample in which the sequence represented by the signal sequence is identical to the portion of the target sequence to be identified.

Thus, the Jones *et al.* published application does not suggest the method of amended claim 13 herein and its combination with the Sorge *et al.* patent correspondingly fails to suggest the method of amended claim 10. The rejection under Section 103(a) should therefore be withdrawn.

Conclusion

The claims as listed are believed to be in condition for allowance and early notice of the same is respectfully requested.

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Respectfully submitted,
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